

Amendments to the Specification:

Please replace the paragraph bridging pages 50-51 with the following amended paragraph:

The chimeric proteins of the present invention can be generated so as to act as either antagonists or agonists to the biological activity of a particular biological ligand. For example, the activity of a number of growth factors can be potentiated by the addition of either heparin or heparan sulfate chains of a proteoglycan and can be used to generate chimeric growth factors with enhanced binding abilities. Exemplary growth factors useful in creating the chimeric syndecan molecules of the present invention include: growth factors of the heparin-binding growth factor (HBGF) family such as basic fibroblast growth factor (bFGF), acidic FGF (aFGF), *Int-2*, *hst/K*-FGF, FGF-5, and FGF-6; heparin-binding EGF-like growth factor (HB-EGF), platelet-derived growth factor (PDGF), transforming growth factor- α factor- β (TGF- β), vascular endothelial growth factor (VEGF), vascular permeability factor (VPF), hepatocyte growth factor; interferon γ ; and Schwannoma-derived growth factor (SDGF), all of which have demonstrated regulation of biological activity by heparin or heparan sulfate. The role of the heparan sulfate glycosaminoglycan chain in regulating the activity of such cytokines is not well defined, but seems to include, as in the case of the HBGFs, conferring such attributes as protection against proteolytic degradation, enhancing chemical stability, and facilitating binding of the growth factor to its cell surface receptor. By way of illustration, a chimeric protein comprising a portion of bFGF and at least a portion of a syndecan containing a heparan sulfate chain can be constructed as described herein. Basic FGF is a heparin-binding polypeptide growth factor that is mitogenic and chemotactic for a variety of cells of mesodermal and neuroectodermal origin. These activities of bFGF are derived from its specific interaction with one or more high affinity receptors (bFGF-R). These integral transmembrane proteins (bFGF-R) have intracellular tyrosine kinase domains and have been identified on 3T3, endothelial, baby hamster, and PC-12 cells. Several *in vitro* studies have demonstrated that both heparin and heparan sulfate protect bFGF from protease digestion or heat/acid inactivation (Burgess et al. (1989) Annu Rev Biochem, 58:575; and Klasbrun (1989) Progress in Growth Factor Res., vol 1, pp207-235, Pergamon Press, Oxford England). Other studies have provided evidence that heparin or

heparan sulfate acts as a cofactor and promotes the binding of bFGF to its high affinity receptor, thereby enhancing mitogenic activity of bFGF. Basic FGF is also known to interact with cell surface and extracellular heparan sulfate proteoglycans, such as syndecan-1 (also termed "low affinity bFGF receptor") and is the proximate source of the heparan sulfate which mediates subsequent binding of bFGF to the high affinity receptor. Expression of a chimeric bFGF/heparan sulfate molecule would be expected to act agonistically, being able to bind the bFGF high affinity receptor and act as a mitogen in an enhanced fashion to wild-type bFGF. A chimeric construct of this type can be therapeutically useful inasmuch as the half-life of the chimeric molecule can be longer than bFGF itself, can further have a higher binding affinity for the bFGF-receptor, and can be chemically stable to otherwise adverse environments.

Please replace the paragraph bridging pages 48-50 with the following amended paragraph:

In addition to those portions of syndecan-1 described above and the novel heparan sulfate attachment sequences identified in the combinatorial assay of the present invention, portions of syndecan-2, syndecan-3, and syndecan-4, as well as any other syndecan homolog, can be used to generate the chimeric molecules of the present invention. By way of illustration, the extracellular domain of each of the syndecans can be used to create a fusion protein, comprising, in the instance of a syndecan-2 fusion protein, the extracellular domain represented by the formula

R-A-E-L-T-S-D-K-D-K-D-M-Y-L-D-N-S-S-I-E-E-A-S-G-V-Y-P-I-D-D-D-D-Y-A-S-A-S-G-S-G-A-D-E-D-V-E-S-P-E-L-T-T-T-R-P-L-P-K-I-L-L-T-S-A-A-P-K-V-E-T-T-T-L-N-I-Q-N-K-I-P-A-Q-T-K-S-P-E-E-T-D-K-E-K-V-N-L-S-D-S-E-R-K-M-D-P-A-E-E-D-T-N-V-Y-T-E-K-H-S-D-S-L-F-K (SEQ ID NO: 9);

or a portion of the extracellular domain such as;

R-A-E-L-T-S-D-K-D-K-D-M-Y-L-D-N-S-S-I-E-E-A-S-G-V-Y-P-I-D-D-D-D-Y-A-S-A-S-G-S-G (amino acids 1-40 of SEQ ID NO: 2) ~~NO: 2~~ NO: 9);

or;

E-E-A-S-G-V-Y-P-I-D-D-D-D-Y-A-S-A-S-G-S-G-A (amino acids 20-41 of SEQ ID NO: 9);

in instance of syndecan-3 chimeric molecules, the extracellular domain represented by the formula;

P-R-A-L-L-S-R-P-C-G-T-K-M-P-A-Q-L-R-G-I-A-V-L-L-L-L-L-S-A-R-A-A-L-A-Q-P-W-R-N-E-N-Y-E-R-P-V-D-L-E-G-S-G-D-D-D-P-F-G-D-D-E-L-D-D-A-Y-S-G-S-G-S-G-Y-F-E-Q-E-S-G-L-E-T-A-V-S-L-T-T-D-T-S-V-P-L-P-T-T-V-A-V-L-P-V-T-L-V-Q-P-M-A-T-P-F-E-L-F-P-T-E-D-T-S-P-E-Q-T-T-S-V-L-Y-I-P-K-I-T-E-A-P-V-I-P-S-W-K-T-T-T-A-S-T-T-A-S-D-S-P-S-T-T-S-T-T-T-T-T-A-A-T-T-T-T-T-T-T-T-I-S-T-T-V-A-T-S-K-P-T-T-T-Q-R-F-L-P-P-F-V-T-K-A-A-T-T-R-A-T-T-L-E-T-P-T-T-S-I-P-E-T-S-V-L-T-E-V-T-T-S-R-L-V-P-S-S-T-A-K-P-R-S-L-P-K-P-S-T-S-R-T-A-E-P-T-E-K-S-T-A-L-P-S-S-P-T-T-L-P-P-T-E-A-P-Q-V-E-P-G-E-L-T-T-V-L-D-S-D-L-E-V-P-T-S-S-G-P-S-G-D-F-E-I-Q-E-E-E-E-T-T-R-P-E-L-G-N-E-V-V-A-V-V-T-P-P-A-A-P-G-L-G-L-N-A-E-P-G-L-I-D-N-T-I-E-S-G-S-S-A-A-Q-L-P-Q-K-N-I-L-E-R (SEQ ID NO: 8)

or a portion of the extracellular domain such as;

P-R-A-L-L-S-R-P-C-G-T-K-M-P-A-Q-L-R-G-I-A-V-L-L-L-L-L-S-A-R-A-A-L-A-Q-P-W-R-N-E-N-Y-E-R-P-V-D-L-E-G-S-G-D-D-D-P-F-G-D-D-E-L-D-D-A-Y-S-G-S-G-S-G-Y-F-E-Q-E-S-G-L-E-T-A-V-S-L-T-T-D-T-S-V-P-L-P-(amino acids 1-95 of SEQ ID NO: 8)

and in the case of syndecan-4 chimeras, the extracellular domain represented by the formula;

E-S-L-R-E-T-E-V-I-D-P-Q-D-L-L-E-G-R-Y-F-S-G-A-L-P-D-D-E-D-V-V-G-P-G-Q-E-S-D-D-F-E-L-S-G-S-G-D-L-D-D-L-E-D-S-M-I-G-P-E-V-V-H-P-L-V-P-L-D-

N-H-I-P-E-R-A-G-S-G-S-Q-V-P-T-E-P-K-K-L-E-E-N-E-V-I-P-K-R-I-S-P-V-E-E-
S-E-D-V-S-N-K-V-S-M-S-S-T-V-Q-G-S-N-I-F-E-R (SEQ ID NO: 6)

or a portion of the extracellular domain such as;

E-S-L-R-E-T-E-V-I-D-P-Q-D-L-L-E-G-R-Y-F-S-G-A-L-P-D-D-E-D-V-V-G-P-G-
Q-E-S-D-D-F-E-L-S-G-S-G (amino acids 1-46 of SEQ ID NO: 6).